

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

What is claimed is:

1. (Currently amended) A method of identifying a candidate branching morphogenesis modulating agent, said method comprising the steps of:
 - (a) providing an assay system comprising a mitogen-activated protein kinase kinase 6 (MAP2K6) polypeptide or nucleic acid;
 - (b) contacting the assay system of step (a) with a candidate test agent under conditions whereby, but for the presence of the test agent, the system provides a reference activity; and
 - (c) detecting a test agent-biased activity of the assay system, wherein a difference between the test agent-biased activity and the reference activity identifies the test agent as a candidate branching morphogenesis modulating agent.
2. (Currently amended) The method of Claim 1₁ wherein the assay system includes a screening assay comprising a MAP2K6 polypeptide, and the candidate test agent is a small molecule modulator having a molecular weight less than 10,000 daltons.
3. (Currently amended) The method of Claim 2₁ wherein the screening assay is a kinase assay.
4. (Currently amended) The method of Claim 1₁ wherein the assay system includes a binding assay comprising an MAP2K6 polypeptide and the candidate test agent is an antibody.
5. (Currently amended) The method of Claim 1₁ wherein the assay system includes an expression assay comprising an MAP2K6 nucleic acid and the candidate test agent is a nucleic acid ~~modulator~~ molecule.

6. (Currently amended) The method of Claim 5_a wherein the nucleic acid ~~modulator~~ molecule is an antisense oligomer.
7. (Currently amended) The method of Claim 6_a wherein the nucleic acid ~~modulator~~ molecule is a phosphorothioate morpholino oligomer (PMO).
8. (Currently amended) The method of Claim 1_a wherein the assay system comprises cultured cells or a nonhuman animal expressing MAP2K6, and wherein the assay system includes an assay that detects an agent-biased change in branching morphogenesis_a.
9. (Currently amended) The method of Claim 8_a wherein the branching morphogenesis is angiogenesis.
10. (Currently amended) The method of Claim 8_a wherein the assay system comprises cultured cells.
11. (Currently amended) The method of Claim 10_a wherein the assay detects an event selected from the group consisting of cell proliferation, cell cycling, apoptosis, tubulogenesis, cell migration, cell sprouting, and response to hypoxic conditions.
12. (Currently amended) The method of Claim 10_a wherein the assay detects tubulogenesis or cell migration or cell sprouting, and wherein the assay system comprises the step of testing the cellular response to stimulation with at least two different pro-angiogenic agents.
13. (Currently amended) The method of Claim 10_a wherein the assay detects tubulogenesis or cell migration, and wherein cells are stimulated with an inflammatory angiogenic agent.
14. (Canceled)
15. (Currently amended) The method of Claim 44 ~~34~~, wherein the assay system includes a matrix implant assay, a xenograft assay, a hollow fiber assay, or a transgenic tumor assay.

16. (Currently amended) The method of Claim 15_a wherein the assay system includes a transgenic tumor assay that includes a mouse comprising a RIP1-Tag2 transgene.

17. (Currently amended) The method of Claim 1, comprising the additional steps of:

(d) providing a second assay system comprising cultured cells or a non-human animal expressing MAP2K6, wherein the second assay system includes a second assay that detects an agent-biased change in an activity associated with branching morphogenesis;

(e) contacting the second assay system with the candidate test agent of (b) ~~or an agent derived therefrom~~ under conditions whereby, but for the presence of the test agent or agent derived therefrom, the system provides a reference activity; and

(f) detecting an agent-biased activity of the second assay system, wherein a difference between the agent-biased activity and the reference activity of the second assay system confirms the candidate test agent ~~or agent derived therefrom~~ as a candidate branching morphogenesis modulating agent, ~~and wherein the second assay system includes a second assay that detects an agent-biased change in an activity associated with branching morphogenesis.~~

18. (Currently amended) The method of Claim 17_a wherein the second assay detects an agent-biased change in an activity associated with angiogenesis.

19. (Currently amended) The method of Claim 17_a wherein the second assay system comprises cultured cells.

20. (Currently amended) The method of Claim 19_a wherein the second assay detects an event selected from the group consisting of cell proliferation, cell cycling, apoptosis, tubulogenesis, cell migration, cell sprouting and response to hypoxic conditions.

21. (Currently amended) The method of Claim 20_a wherein the second assay detects tubulogenesis or cell migration or cell sprouting, and wherein the second assay system comprises the step of testing the cellular response to stimulation with at least two different pro-angiogenic agents.

22. (Currently amended) The method of Claim 20₁ wherein the assay detects tubulogenesis or cell migration, and wherein cells are stimulated with an inflammatory angiogenic agent.
23. (Canceled)
24. (Currently amended) The method of Claim ~~23~~ 35₁ wherein the assay system includes a matrix implant assay, a xenograft assay, a hollow fiber assay, or a transgenic tumor assay.
25. (Currently amended) The method of Claim 24₁ wherein the assay system includes a transgenic tumor assay that includes a mouse comprising a RPI1-Tag2 transgene.
26. (Original) A method of modulating branching morphogenesis in a mammalian cell comprising contacting the cell with an agent that specifically binds a MAP2K6 polypeptide or nucleic acid.
27. (Currently amended) The method of Claim 26₁ wherein the agent is administered to a mammalian animal predetermined to have a pathology associated with branching morphogenesis.
28. (Currently amended) The method of Claim 26₁ wherein the agent is a small molecule modulator having a molecular weight less than 10,000 daltons, a nucleic acid ~~modulator~~ molecule, or an antibody.
29. (Currently amended) The method of Claim 26₁ wherein the branching morphogenesis is angiogenesis₂.
30. (Currently amended) The method of Claim 29₁ wherein tumor cell proliferation is inhibited.

31. (Currently amended) A method for diagnosing ~~a disease~~ cancer in a patient, wherein the cancer is selected from liver, prostate, skin, stomach, and testis cancer, comprising:

(a) obtaining a biological sample from the patient, wherein the biological sample is obtained from the liver, prostate, skin, stomach, or testis;

(b) contacting the sample with a probe for MBM MAP2K6 expression;

(c) comparing results from step (b) with a control; and

(d) determining whether step (c) indicates a likelihood of ~~disease~~ liver, prostate, skin, stomach, or testis cancer.

32. (Canceled)

33. (Canceled)

34. (New) A method of identifying a candidate branching morphogenesis modulating agent, said method comprising the steps of:

(a) providing an assay system comprising a nonhuman animal expressing MAP2K6, wherein the assay system includes an assay that detects an agent-biased change in branching morphogenesis;

(b) contacting the assay system of step (a) with a candidate test agent under conditions whereby, but for the presence of the test agent, the system provides a reference activity; and

(c) detecting a test agent-biased activity of the assay system, wherein a difference between the test agent-biased activity and the reference activity identifies the test agent as a candidate branching morphogenesis modulating agent.

35. (New) A method of identifying a candidate branching morphogenesis modulating agent, said method comprising the steps of:

(a) providing an assay system comprising a MAP2K6 polypeptide or nucleic acid;

(b) contacting the assay system of step (a) with a candidate test agent under conditions whereby, but for the presence of the test agent, the system provides a reference activity;

(c) detecting a test agent-biased activity of the assay system, wherein a difference

between the test agent-biased activity and the reference activity identifies the test agent as a candidate branching morphogenesis modulating agent;

(d) providing a second assay system comprising a non-human animal expressing MAP2K6, wherein the second assay system includes a second assay that detects an agent-biased change in an activity associated with branching morphogenesis;

(e) contacting the second assay system with the candidate test agent of (b) under conditions whereby, but for the presence of the test agent or agent derived therefrom, the system provides a reference activity; and

(f) detecting an agent-biased activity of the second assay system, wherein a difference between the agent-biased activity and the reference activity of the second assay system confirms the candidate test agent as a candidate branching morphogenesis modulating agent.